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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,020	12/19/2001	Esha A. Gangolli	21402-225 (Cura-525)	3246

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EXAMINER	
MITRA, RITA	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 06/30/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/029,020	GANGOLLI ET AL.	
	Examiner	Art Unit	
	Rita Mitra	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9,12-14,39,42 and 50-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5, 9, 12-14, 39, 42 and 50-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Suplimental to enter to page 2 of office action

In view of the papers filed May 20, 2005, the inventorship in this nonprovisional application has been changed by the deletion of David W Anderson, Boldog, Ferenc L., Burgess, Catherine E., aCasman, Stacie J. , Ji Weizhen, Kekuda, Ramesh , Li, Li, Liu, Xiaohong, MacDougall, John R, Malyankar, Uriel M., Patturajan, Meera, Shimkets, Richard A., Smithon, Glennda, Spytek, Kimberly A., Stone, David J., Vernet, Corine A.M. and Zerhusen, Bryan D..

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

RM

DETAILED ACTION

Applicants' Amendment and Response to Office Action mailed August 26 2004, filed on February 15, 2005 is acknowledged. Claims 1-4, 6-8, 10-11, 15-38, 40-41 and 43-49 have been canceled. Claims 9, 39 and 42 have been amended and entered. Therefore, claims 5, 9, 12-14, 39, 42 and 50-59 are currently pending and are under examination.

Response to Amendments and Remarks

Claim Rejections- 35 USC § 112, second paragraph

Claim 10 is canceled thereby rendering the rejection moot.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title"

Claims 5, 9, 12-14, 39, 42 and 50-59 stand/ are rejected under 35 U.S.C. 101 because the specification does not provide either a specific or substantial asserted utility or a well-established utility, and thus, does not support the claimed invention. The claimed nucleic acids are not supported by either a specific asserted utility or a well established utility because the specification fails to assert any utility for the claimed nucleic acids or the encoded proteins and neither the specification as filed nor any art of record disclose or suggest any activity for the claimed nucleic acids or the encoded proteins such that another non-asserted utility would be well established. Note, because the claimed invention is not supported by a specific asserted utility for the reasons set forth above, credibility cannot be assessed. The reasons are as follows:

The specification, on page 10, Table A describes protein designated as NOV4, set forth in SEQ ID NO: 14 encoded by the nucleic acid sequence of SEQ ID NO: 13 (NOV4, Table A) to which the instant invention relates. The NOV4, which has the 8354 of nucleotide sequence of SEQ ID NO: 13 (page 48+, Table 4A) that encodes a

polypeptide having amino acid sequence of SEQ ID NO: 14 (page 50+, Table 4B). The specification further indicates at page 11 that the NOV4 is homologous to the TEN-M4-like family of proteins, thus the NOV4 nucleic acids, polypeptides, antibodies and related compounds will be useful in therapeutic and diagnostic application, which is associated with various diseases and disorders. Examples of many diseases have been listed (page 11-12, 65-67 and 189-192) but the specification does not indicate explicitly the correlation of the role of any composition comprising NOV4 to a specific disease treatment or prevention. Also, a homology to the TEN-M4-like family of proteins does not conclude that NOV4 polynucleotide encoding NOV4 polypeptide would be useful in therapeutic application for the treatment or prevention of cancer, inflammation, neurological disorders, metabolic disorders and other pathologies/disorders (see page 11 first paragraph to page 12, first paragraph). The specification further indicates at page 52 that the Table 4E lists the domain description from DOMAIN analysis results against NOV4, and on the basis of this results specification indicates that the NOV4 sequence has properties similar to those of other proteins known to contain this domain. However, the specification fails to provide any function of these NOV4 sequences containing the said domain.

The rejection has been set forth in the previous office action. In response, Applicants traverse the foregoing rejection and argue (pages 4-5), that under 35 U.S.C. 101 what required is the assertion of a utility that is specific, substantial and credible. Applicants have stated that they have asserted such a utility for the claimed invention in the specification.

The arguments are not persuasive because it should be noted that the claimed subject matter is not supported by a specific utility because the disclosed uses are generally applicable to broad classes of this subject matter. In addition, further characterization of the claimed subject matter would be required to identify or reasonably confirm a "real world" use. In response it has been stated that (see page 4) Applicants assert that the specification teaches at page 229 the highest expression of the claimed gene (Gene CG50301-01) in ovarian cancer. In addition the specification indicates that the level of expression of this gene appears to be increased in some lung and gastric

cancer tissue, while in kidney tissue the expression is slightly higher in normal tissues than in the matched cancer tissue, thus the expression of this gene **could be** of use as a marker to distinguish cancer tissues from the normal tissues. Therefore, Applicants submit that the specification supports that their asserted utility is specific, substantial and credible. The arguments are considered fully but not found persuasive because no evidence is provided to support this assertion that each polynucleotides and polypeptides of the invention is specifically expressed in the said tissues and not in other tissues. How the ovarian cancer tissue, lung and gastric cancer tissue would be differenciated from the kidney cancer tissue on the basis of CG50301 gene expression no matter how weak the expression is in these tissues. How one would be assured in a surgical procedurethat all ovarian tumor tissue has been removed when other tissues are also being marked by the expression of the gene. Therefore, identifying and studying the properties of the claimed subject matter itself or the mechanisms in which the claimed subject matter is involved does not define a "real world" context of use. Thus the asserted utility is not substantial. Further the specification indicates (page 229) that therapeutic inhibition of the activity of the product of this gene, through the use of antibodies, peptides or polypeptides **may be** useful in the treatment of gastric and lung cancer. However, the specification fails to describe therapeutic inhibition of the activity of the product of this gene. The specification fails to provide any activity or function of this gene. Therefore, one skilled in the art should not have to engage in discovering genomics to learn how to use the invention. This situation requires carrying out future additional research to identify or reasonably confirm a "real world" context of use and therefore do not define specific and substantial utility. Therefore, the rejection under 35 U.S.C. 101 remains.

In the instant case, the failure of applicants to specifically identify why the claimed invention is believed to be useful renders the claimed invention deficient under 35 USC 101. No specific biological activity has been identified for the nucleic acid of SEQ ID NO: 13 and the encoded protein set forth in SEQ ID NO: 14 other than the fact that the protein may be a member of the TEN-M4-like family (page 11). The person having ordinary skill in the art would not be able to identify any specific activity for the protein comprising or related to SEQ ID NO: 14 based on its structure alone for the

reasons set forth above. General statements that a composition has an unspecified biological activity or that do not explain why a composition with that activity is believed to be useful fails to set forth a "specific utility." Brenner v. Manson, 383 US 519, 148 USPQ 689 (Sup. Ct.1966) (general assertion of similarities to known compounds known to be useful without sufficient corresponding explanation why claimed compounds are believed to be similarly useful is insufficient under 35 USC 101).

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 5, 9, 12-14, 39, 42 and 50-59 stand/are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial or well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Claims 5, 9, 51-53 and 57-59 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 5, 9, 51-53 and 57-59 stand/are directed to polynucleotide variants of the sequence of SEQ ID NO: 13 encoding the polypeptide of SEQ ID NO: 14. As discussed above, based on the specification (pages 10-12, 48-67) it is unclear what activity the claimed variants possess, what activity the encoded proteins possess and therefore unclear how a person having skill in the art would have used the claimed variants. The specification does not describe the functional properties of these variants, and the structural information is limited. Therefore, how a skilled artisan would know how to use the claimed variants without undue experimentation.

Claim Rejections – 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:
A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 5, and dependent claims 12-14, 39, 42, 50-53 stand/are rejected under 35 USC 102(b) as being anticipated by Schaefer et al. (WO 98/02541, January 22, 1998) for the reasons given in prior office action as below:

Schaefer et al. teach a member of Heregulin superfamily, termed gamma-Heregulin (γ-HRG) from the human breast cancer cell line, MDA-MB-175 (see Abstract, pages 4-6, 15-23, Fig 1); wherein the γ-HRG has a unique N-terminal domain which is not present in other heregulins (page 5). The secretion of γ-HRG leads to the formation of a constitutively active receptor complex and stimulates the growth of these cells in an autocrine manner (abstract). Schaefer's γ-HRG has 99.77% sequence identity to amino acid sequence of residues 1-400 of SEQ ID NO: 14 (see Schaefer et al., "Human gamma-heregulin cDNA," August 17, 1998, frame search result 2, database: N_Geneseq_29Jan04, Accession NO: AAV19251); and has 100% sequence identity to amino acid sequence of residues 450-520 of SEQ ID NO: 14 (see Schaefer et al., "Human gamma-heregulin cDNA clone 20," August 17, 1998, frame search result 1, database: N_Geneseq_29Jan04, Accession NO: AAV19252). Schaefer et al. also teach the polynucleotides encoding the said polypeptides, and variants (page 8) thereof, and uses of such proteins and their production (see Abstract, pages 4-6, 15-23). Schaefer et al.'s variant has 99.5% sequence identity to 1-400 residues of SEQ ID NO: 14, wherein the amino acid residue at position 28 of SEQ ID NO: 14 is Asp (claim 51), at position 64 is Val (claim 52) and at position 76 is Ala (claim 53) (see frame search result 2, Schaefer et al., "Human gamma-heregulin cDNA," August 17, 1998, database: N_Geneseq_29Jan04, Accession NO: AAV19251). Schaefer et al.'s γ-HRG is considered for the polypeptide fragment 1-400 and 450-520 of SEQ ID NO: 14 encoded by the nucleic acid sequence of

claim 5; and the variants are considered for the variants of claims 51-53 of instant application. Schaefer et al. also teach vectors pRK5 or pSV16B, host cells E.coli and CHO (see page 6, 15-16), which are considered for the vectors of claims 12 and 13 and host cells of claim 14; and a composition comprising γ-HRG (page 5) is considered for claim 39 and a kit comprising the said composition (page 36) is considered for the claim 42 of instant application. Thus Schaefer et al. anticipates claims 5, 12-14, 39, 42 and 51-53 of the instant application.

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 USC 102(b) as being anticipated by Oohashi et al. ("Mouse Ten-m/Odz is a new family of dimeric type II transmembrane proteins expressed in many tissues," The J. of Cell Biology, vol 145, No. 3, pp 563-577, May 3, 1999). Oohashi et al. teach a protein that lacks signal peptide but contains a hydrophobic domain after 300-400 amino acids from N-terminus and contain 8 consecutive EGF-like domain to the C-terminal of the hydrophobic domain (see abstract). Oohashi's protein having 98% sequence identity to 750-850 residues of SEQ ID NO: 14 (see frame search result 3, Oohashi et al., "Mus musculus mRNA for Ten-m4," May 8, 1999, database: GenEmbl, Accession NO: AB025413); having 98.1% sequence identity to 1250-1400 residues of SEQ ID NO: 14 (see frame search result 2, Oohashi et al., "Mus musculus mRNA for Ten-m4," May 8, 1999, database: GenEmbl, Accession NO: AB025413); having 99% sequence identity to 1490-1750 residues of SEQ ID NO: 14 (see frame search result 5, Oohashi et al., "Mus musculus mRNA for Ten-m4," May 8, 1999, database: GenEmbl, Accession NO: AB025413) are considered for the fragment sequence 750-850, 1250-1400 and 1490-1750 of SEQ ID 14 of claim 5(e).

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 USC 102(b) as being anticipated by Wang et al. ("Identification of novel stress-induced genes downstream of *chop*," The Embo Journal, vol 17, No. 13, pp 3619-3630, 1998). Wang et al. teach a nuclear protein that dimerizes avidly with members of the C/EBP family of transcription factors (see abstract). Wang's protein having 99.1% sequence identity to 1100-1200 residues of SEQ ID NO: 14 (see frame search result 3, Wang et al., "Mus musculus DOC4 mRNA," August 15, 1998, database: GenEmbl, Accession NO:

AF059485) is considered for the fragment sequence 1100-1200 of SEQ ID 14 of claim 5(e).

Claim 5 and dependent claims 10, 12-14, 39, 42, 50-53 are rejected under 35 USC 102(a) as being anticipated by Nagase et al. ("Prediction of the coding sequences of unidentified human genes. XVI. The complete sequence of 150 new cDNA clones from brain which code for large proteins *in vitro*," DNA Research, vol 7, No. 1, pp 65-73, 2000). Nagase's protein having 100% sequence identity to 1760-2300 residues of SEQ ID NO: 14 (see frame search result 3, Nagase et al., "Homo sapiens mRNA for KIAA1302 protein," May 10, 2002, database: GenEmbl, Accession NO: AB037723); having 100% sequence identity to 2400-2600 residues of SEQ ID NO: 14 (see frame search result 4, Nagase et al., "Homo sapiens mRNA for KIAA1302 protein," May 10, 2002, database: GenEmbl, Accession NO: AB037723); having 100% sequence identity to 2650-2725 residues of SEQ ID NO: 14 (see frame search result 6, Nagase et al., "Homo sapiens mRNA for KIAA1302 protein," May 10, 2002, database: GenEmbl, Accession NO: AB037723) are considered for the fragment sequences 1760-2300, 2400-2600 and 2650-2725 of SEQ ID 14 of claim 5(e).

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any

extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Inquiries

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rita Mitra whose telephone number is (571) 272-0954. The Examiner can normally be reached from 9:30 a.m. to 6:30 p.m. on weekdays. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Jon Weber, can be reached at (571) 272-0925. Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette,1096 OG 30 (November 15, 1989). The Fax Center number is (703) 872-9306. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (571) 272-0547.

JON WEBER
SUPERVISORY PATENT EXAMINER

Rita Mitra, Ph.D.
May 13, 2005